REMARKS

Applicants have amended claims 1 and 55 to recite the preferred antihistamine, epinastine. Applicants have canceled, without prejudice, claims 4-7 and 19-23. The subject matter of those claims may be prosecuted in applications claiming the benefit hereof. Claims 1-3, 8-9, 17-18, 24-25 and 54-56 are presented for examination.

Claims 1-9, 17-25 and 54-56 stand "rejected under 35 U.S.C. 103(a) as being unpatentable over Sarlikiotis et al. (U.S. Pat. No. 6,284,287) in view of Garvey et al. (U.S. Pat. No. 5,824,669)". In particular, though conceding that Sarlikiotis et al. "does not teach a tiotropium salt", it is alleged to "have been obvious to one of ordinary skill in the art at the time the invention was made to use the teachings of Garvey within the teachings of Sarlikiotis because Garvey teaches the use of tiotropium, ipratropium, etc. in the treatment of respiratory diseases and Sarlikiotis teaches the combination of an anticholinergic agent (i. e., ipratropium bromide) with an antihistamine".

Applicants respectfully traverse that rejection.

Claims 1-9, 17-25 and 54-56 stand "rejected under 35 U.S.C. 103(a) as being unpatentable over Garvey et al. (U.S. Patent No. 5,824,669) in view of Naclerio (Clinical and Experimental Allergy -1998). Although conceding that "Garvey is deficient in the sense that he does not teach the combined use of an anticholinergic with an antihistamine", it is alleged that a) Garvey teaches the intranasal administration of anticholinergic agents in compositions containing lactose as an excipient, and b) Naclerio "suggests a synergistic effect" in the use of ipratropium bromide and an antihistamine to treat allergic rhinitis. It is concluded that "it would have been obvious to use an anticholinergic with an antihistamine to treat "respiratory-related diseases and disorders".

Applicants respectfully traverse that rejection.

Claims 1-9, 17-25 and 54-56 stand "rejected under 35 U.S.C. 103(a) as being unpatentable over Naclerio (Clinical and Experimental Allergy – 1998) in view of Garvey et al. (U.S. Pat. No. 5,824,669) and further in view of Sarlikiotis et al. (U.S. Pat. No.

6,284,287). In particular, although conceding that a) "Naclerio ... does not teach tiotropium", and "does not teach the instant excipients", and b) Garvey "does not teach the combined use of an anticholinergic with an antihistamine", and c) Sarlikiotis "does not teach a tiotropium salt", it is alleged to be obvious to select tiotropium from Garvey, combine it with an antihistamine of Naclerio, and the excipients and administration by inhalation of Sarlikiotis to meet the elements of the claimed invention.

Applicants respectfully traverse that rejection.

Applicants' invention relates to the discovery of novel compositions comprising the combination of anticholinergics and antihistamines and their use to treat respiratory diseases. More particularly, the claimed invention relates to the discovery of beneficial composition for treating respiratory diseases comprising tiotropium salt, an antihistamine comprising epinastine, and a saccharide, preferably a mono- and/or disacchartide. It has been discovered, unexpectedly, that, administration of a composition comprising an antihistamine comprising epinastine and a tiotropium salt produces a beneficial effect in the treatment of inflammatory or obstructive diseases.

At the outset, not all chemical agents having anticholinergic activity would be suitable agents to treat respiratory disease. That is, compounds found to exert a reduction of parasympathetic nerve impulses or the selective inhibition of muscarinic (M1-M5) or nicotinic mechanisms, affect a variety of physiologic functions, most notably, in depression and Parkinson's disease (e.g., atropine). Thus, there can be no presumption of a common class effect among anticholinergics in the treatment of respiratory disease. More specifically, the pharmacology of tiotropium (slow onset and offset due to prolonged M3 receptor dissociation in the treatment of respiratory diseases) cannot be predicted from the effects of non-selective binding of ipratropium or oxitropium, particularly, when administered in combination with another active ingredient. Furthermore, that Naclerio refers to the use of ipratropium and an antihistamine other than epinastine to treat allergic rhinitis gives no expectation that the combination of tiotropium and epinastine would be synergistically effective in the treatment of a pulmonary disease such as COPD.

Thus, there is no disclosure or suggestion of combining either a) tiotropium with any antihistamine, or b) any anticholinergic with epinastine. Most importantly, the cited art simply fails to disclose or suggest the use of tiotropium salt with any other active ingredient in the treatment of respiratory disease. Moreover, the physico-chemical interaction between tiotropium salts and antihistamines such as epinastine and their physiologic effects cannot be predicted based on the disclosure of either Garvey or Sarlikiotis. Thus, incorporation of the composition into a kit cannot be rendered obvious.

Moreover, the generic disclosure of all available excipients available to the skilled artisan for producing inhalation powders does not necessarily lead the ordinarily skilled worker to saccharides as excipients useful to provide tiotropium with the beneficial therapeutic distribution characteristics of the claimed clinical combination in the lung.

Given the cited art, it is not obvious that tiotropium salt could be mixed with an antihistamine comprising epinastine and a saccharide excipient to produce a desirable pharmacologic effect in respiratory disease, and not be burdened by biologic or chemical interaction, pharmacologic inhibition, or produce an unacceptable toxicity. Before applicants' invention, it was unknown, and unknowable, whether administration of the claimed composition to a patient would adversely impact the patient, for example, producing unacceptable pulmonary absorption resulting in therapeutic failure or harm.

At most, "An 'obvious-to-try' situation exists when a general disclosure may pique the scientist's curiousity, such that further investigation might be done as a result of the disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain directions were pursued." In re Eli Lilly & Co., 902, F.2d 943, 945, 14 USPQ 2d 1741, 1743 (Fed. Cir. 1990).

In light of the above arguments and remarks, applicants respectfully submit that the pending claims are in condition for allowance.

Early and favorable action on the merits is earnestly solicited.

Respectfully submitted,

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